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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/965,825	10/01/2001	Nicole Dusch	213545US0X	3991

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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.  
1940 DUKE STREET  
ALEXANDRIA, VA 22314

EXAMINER
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RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b>	Application No. 09/965,825	Applicant(s) DUSCH ET AL.	
	Examiner Delia M. Ramirez	Art Unit 1652	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 16 September 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: see attached.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: none.

Claim(s) objected to: none.

Claim(s) rejected: 32-58.

Claim(s) withdrawn from consideration: none.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

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***ADVISORY ACTION***

1. Claims 32-58 are pending.
2. The request for entering amendments to the specification and claims 32, 51, 56-58, adding claims 59-60, canceling claims 33, 35-45, and arguments filed on 9/16/2004 under 37 CFR 1.116 in reply to the Final Action mailed on 6/16/2004 are acknowledged. The proposed amendments to the claims will not be entered. While amendments to the claims seem to overcome the objections, the 35 USC 112, second paragraph rejections, and some of the grounds of rejections previously applied in regard to 35 USC 112, first paragraph, the proposed amendments to the claims raise new issues which would require further consideration as discussed below.
3. Proposed amended claim 56 and new claim 59 would be rejected under 35 U.S.C. 112, second paragraph, due to the recitation of the term "stringent conditions". Absent a statement defining the term, it is unclear as to which polynucleotides are encompassed by the claims in view of the fact that different stringent conditions will result in different polynucleotides hybridizing with the full complement of the polynucleotide of SEQ ID NO: 1 or 4. Also, the specification provides no definition as to the specific conditions which are considered "stringent" in regard to hybridization. It is noted that while the specification has been amended to include a statement of suitable stringent hybridization conditions, this amendment does not provide an explicit definition of what is encompassed by the term. The conditions recited are exemplary and do not limit the meets and bounds of the term. Proposed amended claim 32 has not been rejected in view of the fact that the last sentence in the claim defines the stringent conditions. For examination purposes, proposed amended claim 56 and new claim 59 will be interpreted as reciting "any hybridization conditions".
4. Claim 52 would be rejected under 35 U.S.C. 112, second paragraph, due to the recitation of the term "the process of claim 50 wherein the panB, panC, ilvC and ilvD genes.." as there is no antecedent

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basis for the terms "panB, panC, ilvC and ilvD genes" in claim 50 or claim 32 (from which claim 50 depends). For examination purposes, claim 52 will be interpreted as reciting "the process of claim 51".

5. Proposed amended claim 32, 51, 56-58, claims 46-50, 52-55, and new claims 59-60 would be rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Proposed amended claims 32, 56-58, claims 46-50, 52-55, and new claims 58-60 are directed in part to a process for the production of D-pantothenic acid in Coryneform bacteria modified such that the expression of the poxB gene product is reduced in any way, wherein the poxB gene in the Coryneform bacteria prior to being modified either (a) comprises SEQ ID NO:1 or 4, (b) hybridizes under any conditions to the full complement of the polynucleotide of SEQ ID NO:1 or SEQ ID NO:4. Proposed amended claim 51 is directed to the process of proposed amended claim 32, as described above, wherein at least one of the Coryneform bacterium panB, panC, ilvC, or ilvD gene products are increased in any way. See above regarding interpretation of proposed amended claim 56 and new claim 59. As indicated in the Final Action mailed on 6/16/2004, while the specification describes the inactivation of the *C. glutamicum* poxB gene by a deletion in the poxB gene and increased expression of *C. glutamicum* panB, panC, ilvC and ilvD genes by using a strong promoter, the specification fails to describe (1) other methods to reduce expression of any poxB gene from Coryneform bacteria such as modifications in the regulatory region of any Coryneform B poxB gene, (2) other methods to increase expression of any panB, panC, ilvC, or ilvD Coryneform bacteria gene, such as modifications in the regulatory region of those genes, and (3) the structures of other poxB genes from any Coryneform bacteria which would hybridize under any conditions to the polynucleotides of SEQ ID NO:1 or 4. The claimed invention requires a genus of modifications to the recited genes which are unknown. Furthermore, the structural feature as interpreted, i.e. hybridization under any

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conditions to the polynucleotides of SEQ ID NO: 1 or 4, which is shared by all members of the genus of poxB genes prior to modification, does not constitute a substantial portion of the genus as the remainder of any nucleic acid comprising said structural elements is completely undefined and the specification does not define the remaining structural features for members of the genus to be selected. Therefore, one cannot reasonably conclude that the claimed method is adequately described.

6. Proposed amended claims 32, 51, 56-58, claims 34, 46-50, 52-55, and new claims 59-60 would be rejected under 35 USC 112, first paragraph, because the specification while being enabling for (1) a process for the production of D-pantothenic acid in *C. glutamicum* by inactivating the *C. glutamicum* poxB gene or a Coryneform bacterium wherein the wild-type poxB gene comprises SEQ ID NO:1 or SEQ ID NO:4, wherein said inactivation occurs by a deletion in the poxB gene, and (2) a process as described above, wherein at least one of the *C. glutamicum* panB, panC, ilvC, or ilvD gene products are increased by overexpressing the panB, panC, ilvC, or ilvD genes by using a strong promoter, does not reasonably provide enablement for (a) a process for the production of D-pantothenic acid in Coryneform bacteria modified such that the expression of the poxB gene product is reduced in any way, wherein the poxB gene in the Coryneform bacteria prior to being modified (1) hybridizes under any conditions to the full complement of the polynucleotide of SEQ ID NO: 1 or 4, or (2) hybridizes to the full complement of the polynucleotide of SEQ ID NO: 1 or 4 at conditions requiring washing in 5xSSC at a temperature of from 50-68 C, or (b) the process of (a) wherein at least one of the Coryneform bacterium panB, panC, ilvC, or ilvD gene products are increased in any way. The specification does not enable any person skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Proposed amended claims 32, 56-58, claims 46-50, 52-55, and new claims 58-60 are directed in part to a process for the production of D-pantothenic acid in Coryneform bacteria modified such that the expression of the poxB gene product is reduced in any way, wherein the poxB gene in the Coryneform

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bacteria prior to being modified either (a) comprises SEQ ID NO:1 or 4, or (b) hybridizes under any conditions to the full complement of the polynucleotide of SEQ ID NO:1 or SEQ ID NO:4. Proposed amended claim 51 is directed to the process of proposed amended claim 32, as described above, wherein at least one of the Coryneform bacterium panB, panC, ilvC, or ilvD gene products are increased in any way. See above regarding interpretation of proposed amended claim 56 and new claim 59. Claim 34 is directed in part to a process for the production of D-pantothenic acid in Coryneform bacteria modified such that the expression of the poxB gene product is eliminated, wherein the poxB gene in Coryneform bacteria prior to being modified comprises a polynucleotide which hybridizes to the full complement of the polynucleotide of SEQ ID NO: 1 or 4 at conditions which require washing in 5xSSC at a temperature of from 50-68 C. As indicated above, the specification is silent in regard to other methods to reduce expression of any poxB gene from Coryneform bacteria such as modifications in the regulatory region of any Coryneform B poxB gene, other methods to increase expression of any panB, panC, ilvC, or ilvD Coryneform bacteria gene, such as modifications in the regulatory region of those genes, the structures of other poxB genes from any Coryneform bacteria which would hybridize under any conditions to the polynucleotides of SEQ ID NO:1 or 4, or the critical structural elements in the polynucleotides of SEQ ID NO: 1 or 4 required in any poxB gene which hybridizes at the washing conditions recited. It is noted that the conditions recited, are those of high salt and low temperature (with the exception of 68 C). Therefore, polynucleotides having low structural homology to the polynucleotides of SEQ ID NO:1 or 4 would be included in the genus recited. As indicated in the Final Action mailed on 6/16/2004, the art teaches the unpredictability of isolating polynucleotides encoding polypeptides of similar function based solely on structural homology. See, particularly, the teachings of Witkowski et al. and Seffernick et al., wherein even structural homologs having more than 95% sequence identity were found to have different function. Furthermore, it is reiterated herein that the claimed method requires a genus of modifications to the recited genes such that their expression is reduced or enhanced which are unknown. Therefore, one

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cannot reasonably conclude that the full scope of the claimed invention is enabled by the instant disclosure.

7. The rejections previously applied are, therefore, maintained for the reasons of record in view of the non-entry of the proposed amendments.

8. For purposes of Appeal, the status of the claims is as follows:

Claim(s) allowed: NONE

Claims(s) objected to: NONE

Claim(s) rejected: 32-58

Claim(s) withdrawn from consideration: NONE

9. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or

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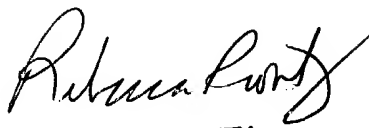
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relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.  
Patent Examiner  
Art Unit 1652

DR  
October 12, 2004

  
REBECCA E. PROUTY  
PRIMARY EXAMINER  
GROUP ~~1800~~  
1600